

DOCKET NO.: JANS-0026 (JAB-1499 US)

PATENT

Application No.: 10/019,380

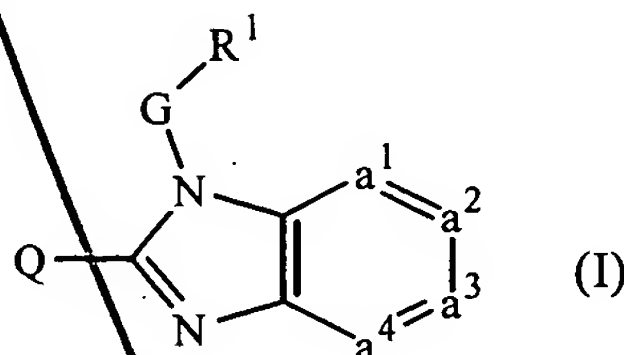
Office Action Dated: April 18, 2003

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1. (currently amended)

A compound of formula



a prodrug, N-oxide, addition salt, quaternary amine, metal complex or stereochemically isomeric form thereof wherein

$-a^1=a^2-a^3=a^4-$  represents a bivalent radical of formula

$-\text{CH}=\text{CH}-\text{CH}=\text{CH}-$  (a-1);

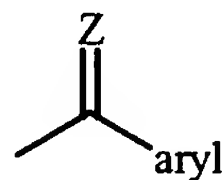
$-\text{N}=\text{CH}-\text{CH}=\text{CH}-$  (a-2);

$-\text{CH}=\text{N}-\text{CH}=\text{CH}-$  (a-3);

$-\text{CH}=\text{CH}-\text{N}=\text{CH}-$  (a-4); or

$-\text{CH}=\text{CH}-\text{CH}=\text{N}-$  (a-5);

wherein each hydrogen atom in the radicals (a-1), (a-2), (a-3), (a-4) and (a-5) may optionally be replaced by halo,  $\text{C}_{1-6}$ alkyl, nitro, amino, hydroxy,  $\text{C}_{1-6}$ alkyloxy, polyhalo $\text{C}_{1-6}$ alkyl, carboxyl, amino $\text{C}_{1-6}$ alkyl, mono- or di( $\text{C}_{1-4}$ alkyl)amino $\text{C}_{1-6}$ alkyl,  $\text{C}_{1-6}$ alkyloxycarbonyl, hydroxy $\text{C}_{1-6}$ alkyl, or a radical of formula

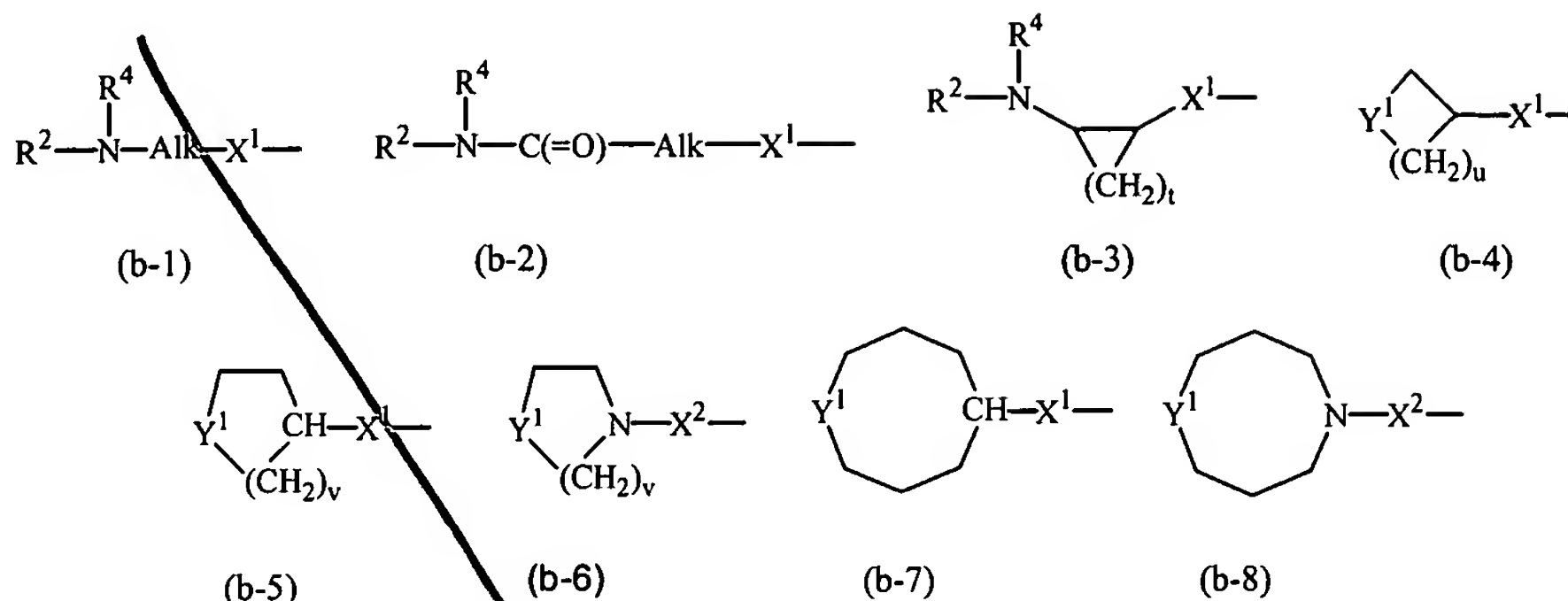


wherein  $=\text{Z}$  is  $=\text{O}$ ,  $=\text{CH}-\text{C}(=\text{O})-\text{NR}^{5a}\text{R}^{5b}$ ,  $=\text{CH}_2$ ,  $=\text{CH}-\text{C}_{1-6}\text{alkyl}$ ,  $=\text{N}-\text{OH}$  or  $=\text{N}-\text{O}-\text{C}_{1-6}\text{alkyl}$ ;

Q is a radical of formula

C1

Q1  
cont



wherein Alk is C<sub>1-6</sub>alkanediyl;

Y<sup>1</sup> is a bivalent radical of formula -NR<sup>2</sup>- or -CH(NR<sup>2</sup>R<sup>4</sup>)-;

X<sup>1</sup> is NR<sup>4</sup>, S, S(=O), S(=O)<sub>2</sub>, O, CH<sub>2</sub>, C(=O), C(=CH<sub>2</sub>), CH(OH), CH(CH<sub>3</sub>), CH(OCH<sub>3</sub>), CH(SCH<sub>3</sub>), CH(NR<sup>5a</sup>R<sup>5b</sup>), CH<sub>2</sub>-NR<sup>4</sup> or NR<sup>4</sup>-CH<sub>2</sub>;

X<sup>2</sup> is a direct bond, CH<sub>2</sub>, C(=O), NR<sup>4</sup>, C<sub>1-4</sub>alkyl-NR<sup>4</sup>, NR<sup>4</sup>-C<sub>1-4</sub>alkyl;

t is 2, 3, 4 or 5;

u is 1, 2, 3, 4 or 5;

v is 2 or 3; and

whereby each hydrogen atom in Alk and the carbocycles and the heterocycles defined in radicals (b-3), (b-4), (b-5), (b-6), (b-7) and (b-8) may optionally be replaced by R<sup>3</sup>; with the proviso that when R<sup>3</sup> is hydroxy or C<sub>1-6</sub>alkyloxy, then R<sup>3</sup> can not replace a hydrogen atom in the  $\alpha$  position relative to a nitrogen atom;

G is C<sub>1-10</sub>alkanediyl substituted with one or more hydroxy, C<sub>1-6</sub>alkyloxy, arylC<sub>1-6</sub>alkyloxy, C<sub>1-6</sub>alkylthio, arylC<sub>1-6</sub>alkylthio, HO(-CH<sub>2</sub>-CH<sub>2</sub>-O)<sub>n</sub>-, C<sub>1-6</sub>alkyloxy (-CH<sub>2</sub>-CH<sub>2</sub>-O)<sub>n</sub>- or arylC<sub>1-6</sub>alkyloxy(-CH<sub>2</sub>-CH<sub>2</sub>-O)<sub>n</sub>-;

R<sup>1</sup> is a monocyclic heterocycle or aryl; said heterocycle being selected from piperidinyl, piperazinyl, pyridyl, pyrazinyl, pyridazinyl, pyrimidinyl, furanyl, tetrahydrofuranyl, thienyl, pyrrolyl, thiazolyl, oxazolyl, imidazolyl, isothiazolyl, pyrazolyl, isoxazolyl, oxadiazolyl; and each heterocycle may optionally be substituted with 1 or where possible more, such as 2, 3 or 4, substituents selected from halo, hydroxy, amino, cyano, carboxy, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkyloxy, C<sub>1-6</sub>alkylthio,

DOCKET NO.: JANS-0026 (JAB-1499 US)

PATENT

Application No.: 10/019,380

Office Action Dated: April 18, 2003

C'  
D'  
Cont

C<sub>1-6</sub>alkyloxyC<sub>1-6</sub>alkyl, aryl, arylC<sub>1-6</sub>alkyl, arylC<sub>1-6</sub>alkyloxy, hydroxyC<sub>1-6</sub>alkyl, mono- or di(C<sub>1-6</sub>alkyl)amino, mono- or di(C<sub>1-6</sub>alkyl)aminoC<sub>1-6</sub>alkyl, polyhaloC<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkylcarbonylamino, C<sub>1-6</sub>alkyl-SO<sub>2</sub>-NR<sup>5c</sup>-, aryl-SO<sub>2</sub>-NR<sup>5c</sup>-, C<sub>1-6</sub>alkyloxycarbonyl, -C(=O)-NR<sup>5c</sup>R<sup>5d</sup>-, HO(-CH<sub>2</sub>-CH<sub>2</sub>-O)<sub>n</sub>-, halo(-CH<sub>2</sub>-CH<sub>2</sub>-O)<sub>n</sub>-, C<sub>1-6</sub>alkyloxy(-CH<sub>2</sub>-CH<sub>2</sub>-O)<sub>n</sub>-, arylC<sub>1-6</sub>alkyloxy(-CH<sub>2</sub>-CH<sub>2</sub>-O)<sub>n</sub>- and mono- or di(C<sub>1-6</sub>alkyl)amino (-CH<sub>2</sub>-CH<sub>2</sub>-O)<sub>n</sub>;

each n independently is 1, 2, 3 or 4;

R<sup>2</sup> is hydrogen, formyl, C<sub>1-6</sub>alkylcarbonyl, Hetcarbonyl, pyrrolidinyl, piperidinyl, homopiperidinyl, C<sub>3-7</sub>cycloalkyl substituted with N(R<sup>6</sup>)<sub>2</sub>, or C<sub>1-10</sub>alkyl substituted with N(R<sup>6</sup>)<sub>2</sub> and optionally with a second, third or fourth substituent selected from amino, hydroxy, C<sub>3-7</sub>cycloalkyl, C<sub>2-5</sub>alkanediyl, piperidinyl, mono- or di(C<sub>1-6</sub>alkyl)amino, C<sub>1-6</sub>alkyloxycarbonylamino, aryl and aryloxy;

R<sup>3</sup> is hydrogen, hydroxy, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkyloxy, arylC<sub>1-6</sub>alkyl or arylC<sub>1-6</sub>alkyloxy;

R<sup>4</sup> is hydrogen, C<sub>1-6</sub>alkyl or arylC<sub>1-6</sub>alkyl;

R<sup>5a</sup>, R<sup>5b</sup>, R<sup>5c</sup> and R<sup>5d</sup> each independently are hydrogen or C<sub>1-6</sub>alkyl; or

R<sup>5a</sup> and R<sup>5b</sup>, or R<sup>5c</sup> and R<sup>5d</sup> taken together form a bivalent radical of formula -(CH<sub>2</sub>)<sub>s</sub>- wherein s is 4 or 5;

R<sup>6</sup> is hydrogen, C<sub>1-4</sub>alkyl, formyl, hydroxyC<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkylcarbonyl or C<sub>1-6</sub>alkyloxycarbonyl;

aryl is phenyl or phenyl substituted with 1 or more, ~~such as 2, 3 or 4,~~ substituents selected from halo, hydroxy, C<sub>1-6</sub>alkyl, hydroxyC<sub>1-6</sub>alkyl, polyhaloC<sub>1-6</sub>alkyl, and C<sub>1-6</sub>alkyloxy; and

Het is pyridyl, pyrimidinyl, pyrazinyl, or pyridazinyl.

2. (previously amended) A compound according to claim 1, wherein -a<sup>1</sup>=a<sup>2</sup>-a<sup>3</sup>=a<sup>4</sup>- is a radical of formula (a-1) or (a-2).

- C'  
D'  
cont
3. *(previously amended)* A compound according to claim 1, wherein R<sup>1</sup> is phenyl optionally substituted with halo, C<sub>1-6</sub>alkyl or C<sub>1-4</sub>alkyloxy; or pyridyl optionally substituted with 1 or more substituents selected from arylC<sub>1-6</sub>alkyloxy, C<sub>1-6</sub>alkyloxyC<sub>1-6</sub>alkyl, aryl, mono-or di(C<sub>1-6</sub>alkyl)amino, C(=O)-NR<sup>5c</sup>R<sup>5d</sup>, halo or C<sub>1-6</sub>alkyl.
4. *(previously amended)* A compound according to claim 1, wherein G is C<sub>1-4</sub>alkanediyl substituted with hydroxy, C<sub>1-6</sub>alkyloxy, HO(-CH<sub>2</sub>-CH<sub>2</sub>-O)<sub>n</sub>-, C<sub>1-6</sub>alkyloxy(-CH<sub>2</sub>-CH<sub>2</sub>-O)<sub>n</sub>- or arylC<sub>1-6</sub>alkyloxy(-CH<sub>2</sub>-CH<sub>2</sub>-O)<sub>n</sub>-.
5. *(previously amended)* A compound according to claim 1, wherein Q is a radical of formula (b-5) wherein v is 2 and Y<sup>1</sup> is -NR<sup>2</sup>-.
6. *(previously amended)* A compound according to claim 1, wherein X<sup>1</sup> is NH or CH<sub>2</sub>.
7. *(previously amended)* A compound according to claim 1, wherein R<sup>2</sup> is hydrogen or C<sub>1-10</sub>alkyl substituted with NHR<sup>6</sup> wherein R<sup>6</sup> is hydrogen or C<sub>1-6</sub>alkyloxycarbonyl.
8. *(original)* A compound according to claim 1, wherein the compound is [(A),(S)]-N-[1-(2-amino-3-methylbutyl)-4-piperidiny]-1-[(6-bromo-2-pyridinyl)ethoxymethyl]-1H-benzimidazol-2-amine; [(A),(S)]-N-[1-(2-aminopropyl)-4-piperidiny]-1-[ethoxy(6-methyl-2-pyridinyl)methyl]-1H-benzimidazol-2-amine (compound 75); (±)-N-[1-(2-amino-3-methylbutyl)-4-piperidiny]-1-[(2-methoxyethoxy)(6-methyl-2-pyridinyl)methyl]-1H-benzimidazol-2-amine; N-[1-(2-amino-3-methylbutyl)-4-piperidiny]-6-chloro-1-[(2-methoxyethoxy)(6-methyl-2-pyridinyl)methyl]-4-methyl-1H-benzimidazol-2-amine trihydrochloride trihydrate; [(A),(R)]-N-[1-(2-amino-3-methylbutyl)-4-piperidiny]-1-[ethoxy(6-methyl-2-pyridinyl)methyl]-1H-benzimidazol-2-amine monohydrate; (±)-N-[1-(2-

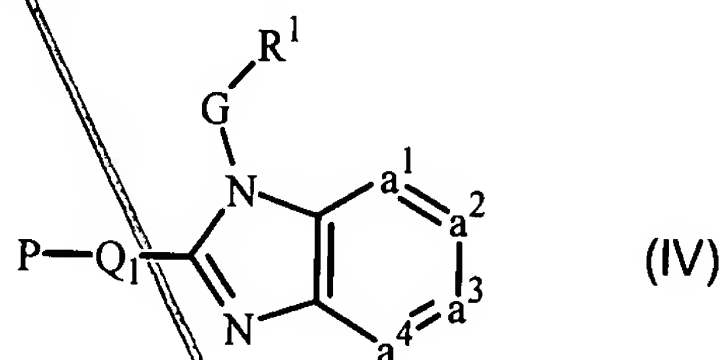
C1  
91  
cont

aminopropyl)-4-piperidinyl]-1-[ethoxy(6-methyl-2-pyridinyl)methyl]-1H-benzimidazol-2-amine; [(A)(S)]-N-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-1-[ethoxy(6-methyl-2-pyridinyl)methyl]-1H-benzimidazol-2-amine monohydrate; (±)-N-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-1-[ethoxy(6-methyl-2-pyridinyl)methyl]-1H-benzimidazol-2-amine; [(A),(R)]-N-[1-(2-aminopropyl)-4-piperidinyl]-1-[ethoxy(6-methyl-2-pyridinyl)methyl]-1H-benzimidazol-2-amine monohydrate; (±)-N-[1-(2-aminoethyl)-4-piperidinyl]-1-[(6-bromo-2-pyridinyl)ethoxymethyl]-2-benzimidazol-2-amine; (±)-N-[1-(2-aminoethyl)-4-piperidinyl]-1-[(2-ethoxyethoxy)(6-methyl-2-pyridinyl)methyl]-1H-benzimidazol-2-amine; [(B),(S)] N-[1-(2-aminopropyl)-4-piperidinyl]-1-[ethoxy(6-methyl-2-pyridinyl)methyl]-1H-benzimidazol-2-amine monohydrate; (±)-N-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-3-[(2-methoxyethoxy)(6-methyl-2-pyridinyl)methyl]-7-methyl-3H-imidazo[4,5-b]pyridin-2-amine; (±)-N-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-1-[(2-ethoxyethoxy)(6-phenyl-2-pyridinyl)methyl]-1H-benzimidazol-2-amine; (±)-N-[1-(2-aminoethyl)-4-piperidinyl]-1-[(2-methoxyethoxy)(6-methyl-2-pyridinyl)methyl]-1H-benzimidazol-2-amine; (±)-N-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-1-[(6-bromo-2-pyridinyl)ethoxymethyl]-4-methyl-1H-benzimidazol-2-amine monohydrate; [(A),(R)]-N-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-1-[(6-bromo-2-pyridinyl)ethoxymethyl]-1H-benzimidazol-2-amine; (±)-N-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-1-[(6-bromo-2-pyridinyl)ethoxymethyl]-1H-benzimidazol-2-amine; a prodrug, N-oxide, addition salt, quaternary amine, metal complex or stereochemically isomeric form thereof.

9. (currently amended) A method of ~~using as a medicine~~ treating a viral infection, comprising the step of administering a therapeutically effective amount of a compound as claimed in any one of claims 1 to 8.

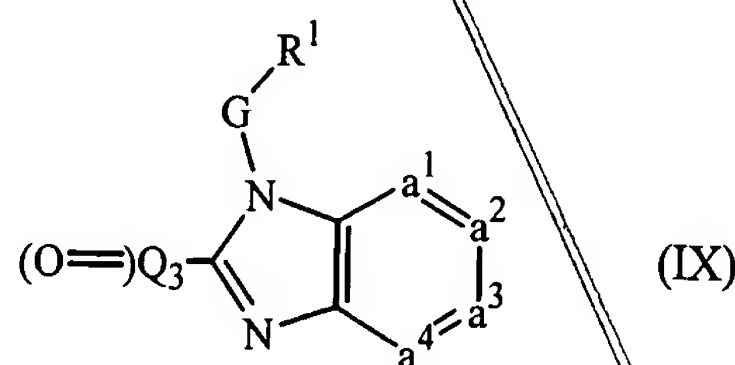
- C/
10. *(previously amended)* A pharmaceutical composition, comprising a pharmaceutically acceptable carrier, and as active ingredient a therapeutically effective amount of a compound as claimed in any one of claims 1 to 8.
11. *(previously amended)* A process of preparing a composition as claimed in claim 10, comprising the step of intimately mixing said carrier with said compound.

12. *(original)* An intermediate of formula



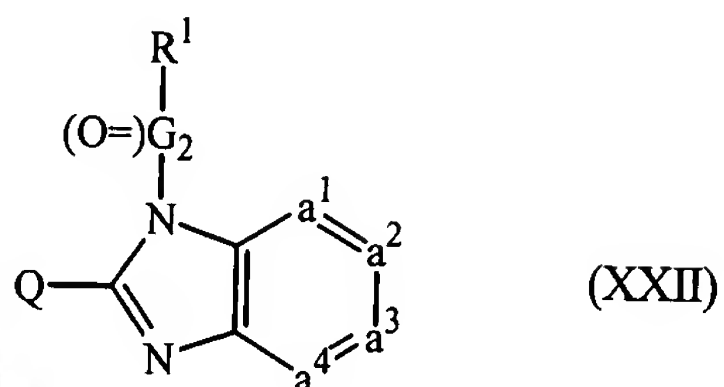
with  $R^1$ , G and  $-a^1=a^2-a^3=a^4-$  defined as in claim 1, P being a protective group, and  $Q_1$  being defined as Q according to claim 1 provided that it is devoided of the  $R^2$  or  $R^6$  substituent.

13. *(original)* An intermediate of formula



with  $R^1$ , G and  $-a^1=a^2-a^3=a^4-$  defined as in claim 1, and  $(O=)Q_3$  being a carbonyl derivative of Q, said Q being defined according to claim 1, provided that it is devoided of the  $-NR^2R^4$  or  $-NR^2-$  substituent.

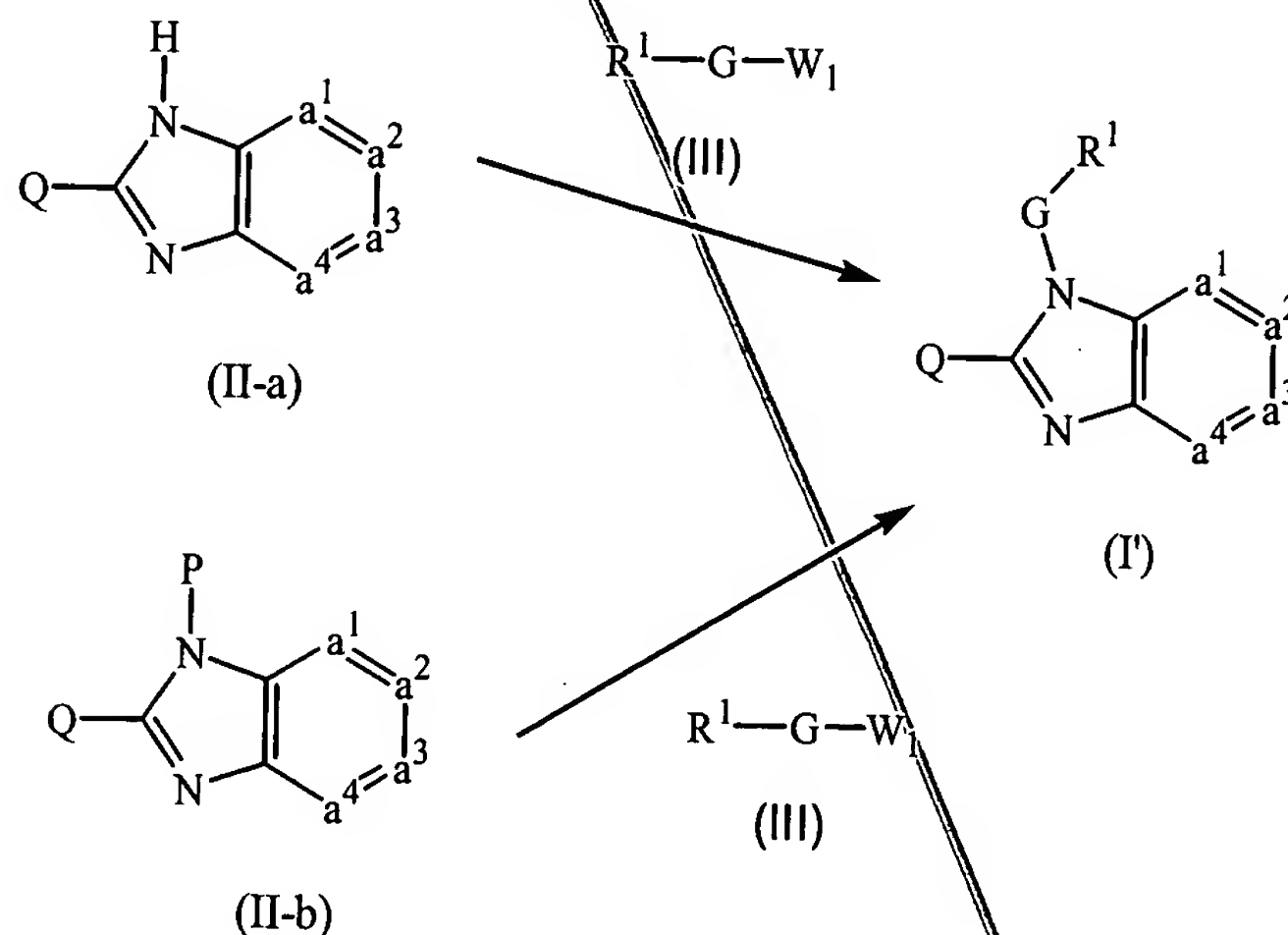
14. *(original)* An intermediate of formula



with  $R^1$ , Q and  $-a^1=a^2-a^3=a^4-$  defined as in claim 1, and  $(O=G_2)$  being a carbonyl derivative of G, said G being defined according to claim 1.

15. (currently amended) A process of preparing a compound as claimed in claim 1, comprising at least one step selected from the group consisting of:

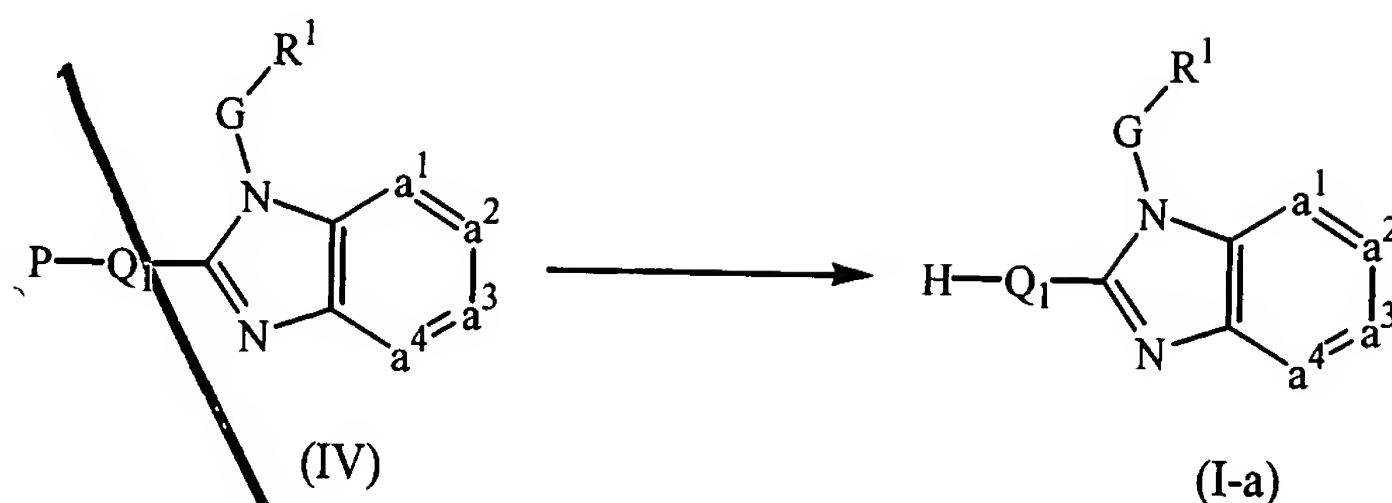
- a) reacting an intermediate of formula (II-a) or (II-b) with an intermediate of formula (III)



with  $R^1$ , G, Q and  $-a^1=a^2-a^3=a^4-$  defined as in claim 1, and  $W_1$  being a **suitable** leaving group, in the presence of a **suitable** base and in a **suitable** reaction-inert solvent;

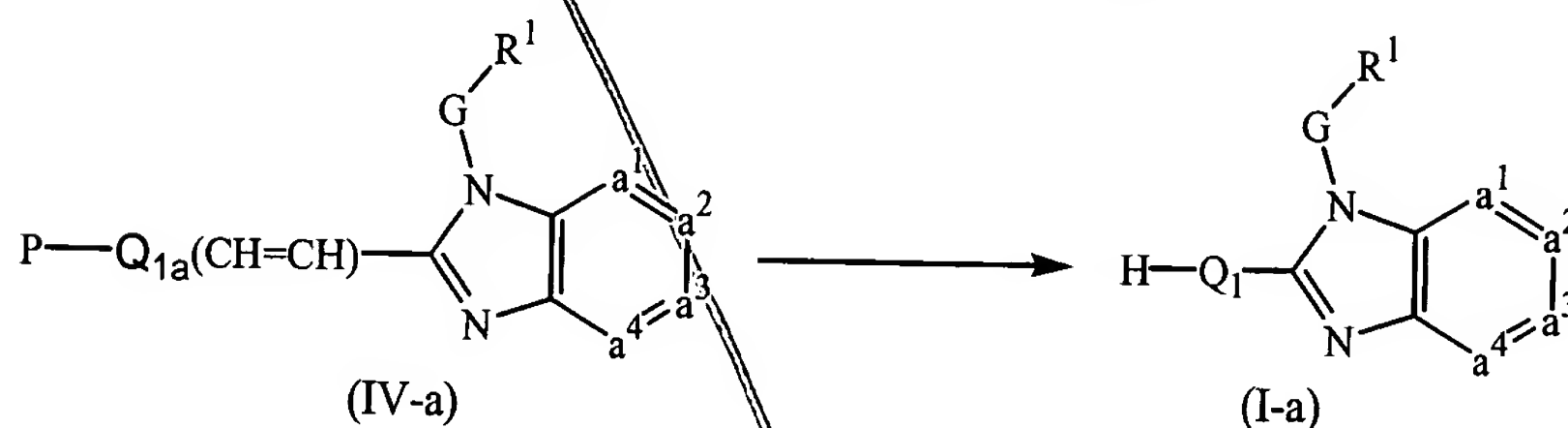
- b) deprotecting an intermediate of formula (IV)

C1  
 D1  
 Cont



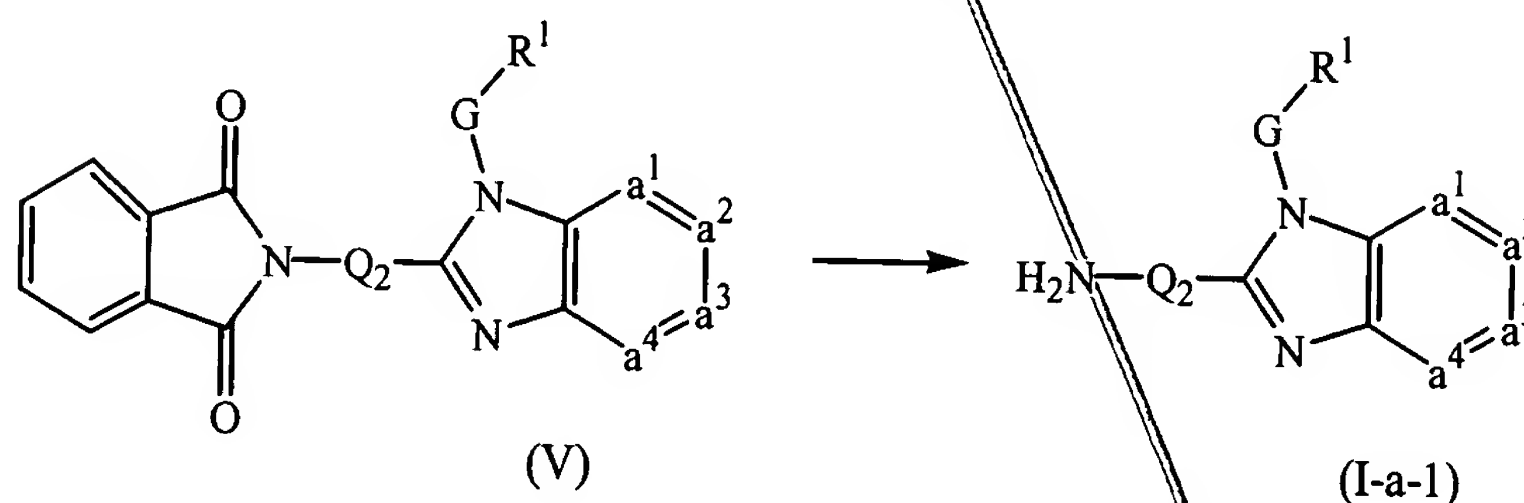
with  $R^1$ , G, and  $-a^1=a^2-a^3=a^4-$  defined as in claim 1, H-Q<sub>1</sub> being defined as Q according to claim 1 provided that R<sup>2</sup> or at least one R<sup>6</sup> substituent is hydrogen, and P being a protective group;

- c) deprotecting and reducing an intermediate of formula (IV-a)



with  $R^1$ , G, and  $-a^1=a^2-a^3=a^4-$  defined as in claim 1, H-Q<sub>1</sub> being defined as Q according to claim 1 provided that R<sup>2</sup> or at least one R<sup>6</sup> substituent is hydrogen, Q<sub>1a</sub>(CH=CH) being defined as Q<sub>1</sub> provided that Q<sub>1</sub> comprises an unsaturated bond, and P being a protective group;

- d) deprotecting an intermediate of formula (V)

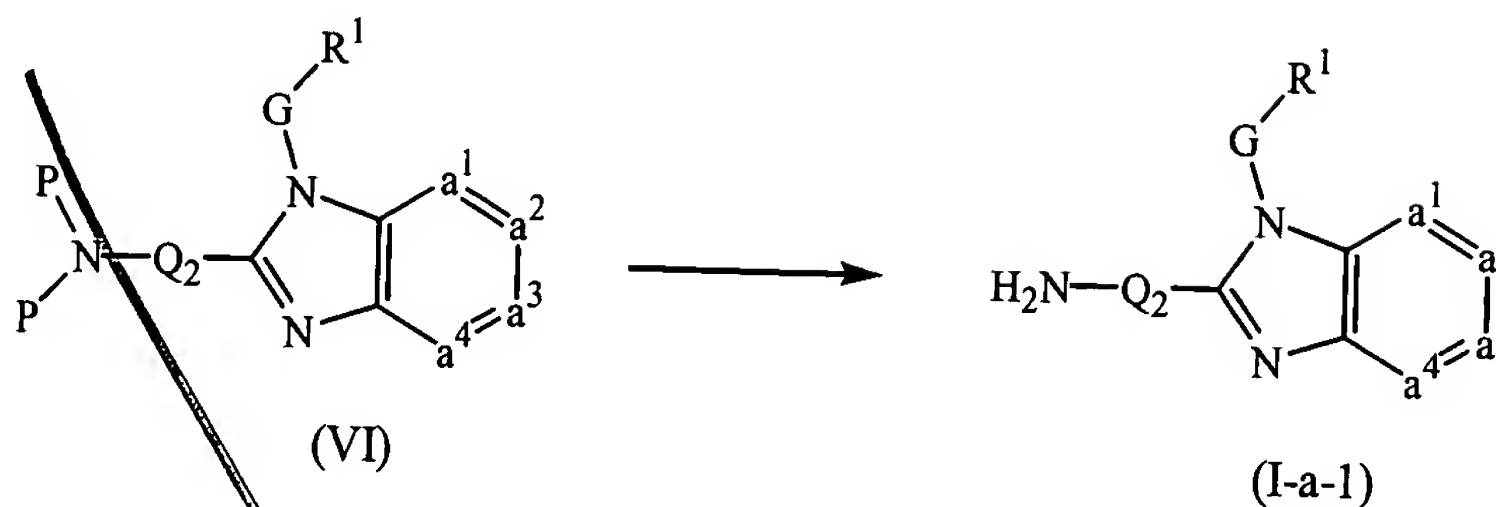


with  $R^1$ , G, and  $-a^1=a^2-a^3=a^4-$  defined as in claim 1, and H<sub>2</sub>N-Q<sub>2</sub> being defined as Q according to claim 1 provided that both R<sup>6</sup> substituents are hydrogen or R<sup>2</sup> and R<sup>4</sup> are both hydrogen;

- e) deprotecting an intermediate of formula (VI)

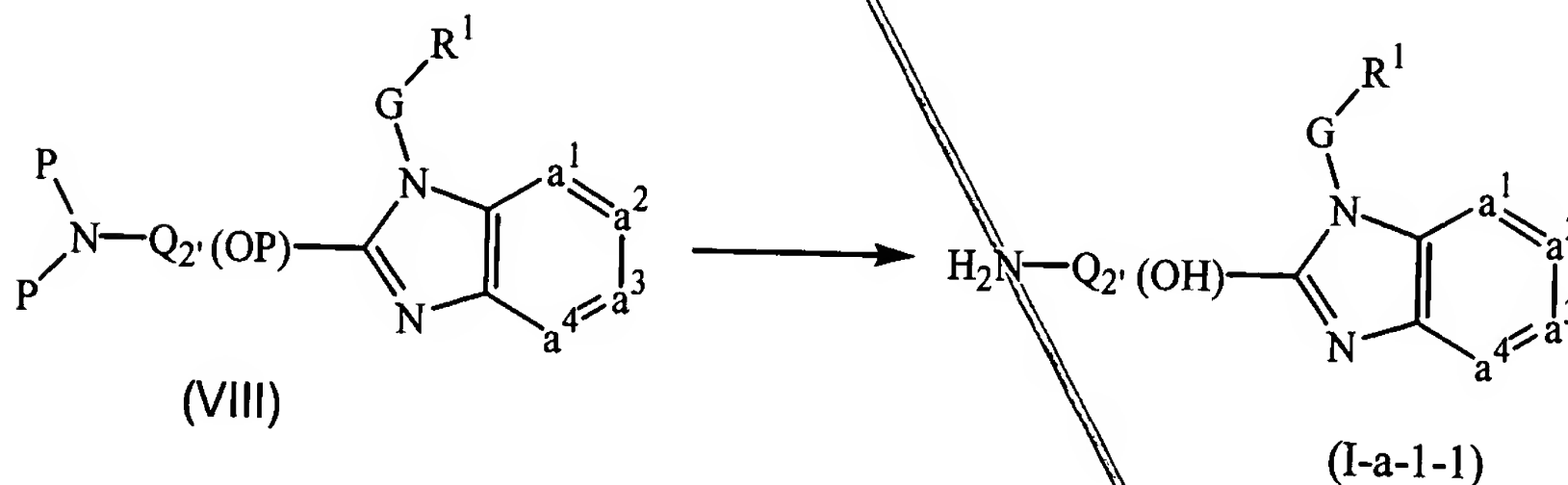
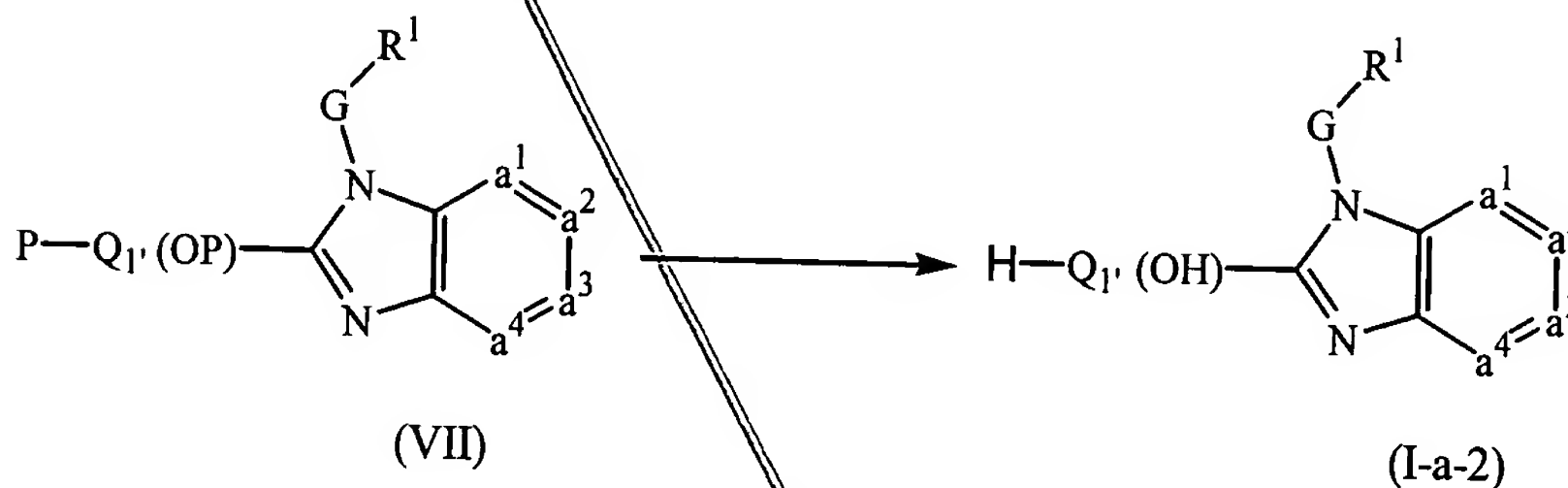


C'  
D'  
Cont



with  $R^1$ , G, and  $-a^1=a^2-a^3=a^4-$  defined as in claim 1, and  $H_2N-Q_2$  being defined as Q according to claim 1 provided that both  $R^6$  substituents are hydrogen or  $R^2$  and  $R^4$  are both hydrogen, and P being a protective group;

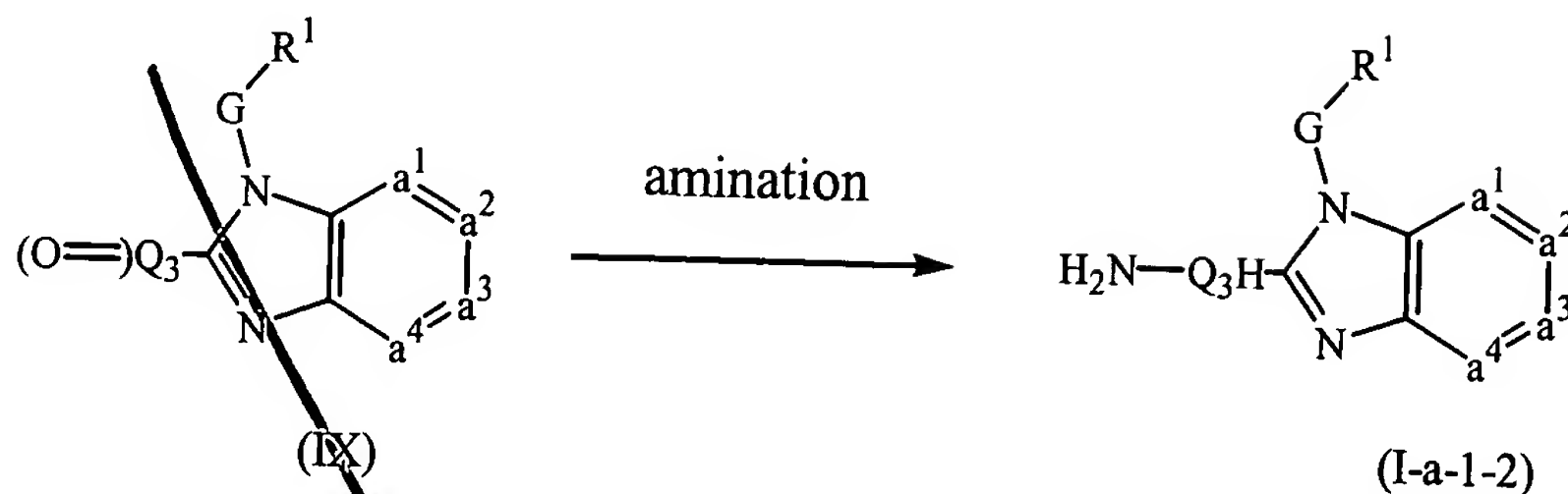
f) deprotecting an intermediate of formula (VII) or (VIII)



with  $R^1$ , G, and  $-a^1=a^2-a^3=a^4-$  defined as in claim 1,  $H-Q_1'(OH)$  being defined as Q according to claim 1 provided that  $R^2$  or at least one  $R^6$  substituent is hydrogen and provided that Q comprises a hydroxy moiety,  $H_2N-Q_2'(OH)$  being defined as Q according to claim 1 provided that both  $R^6$  substituents are hydrogen or  $R^2$  and  $R^4$  are both hydrogen and provided that Q comprises a hydroxy moiety, and P being a protective group;

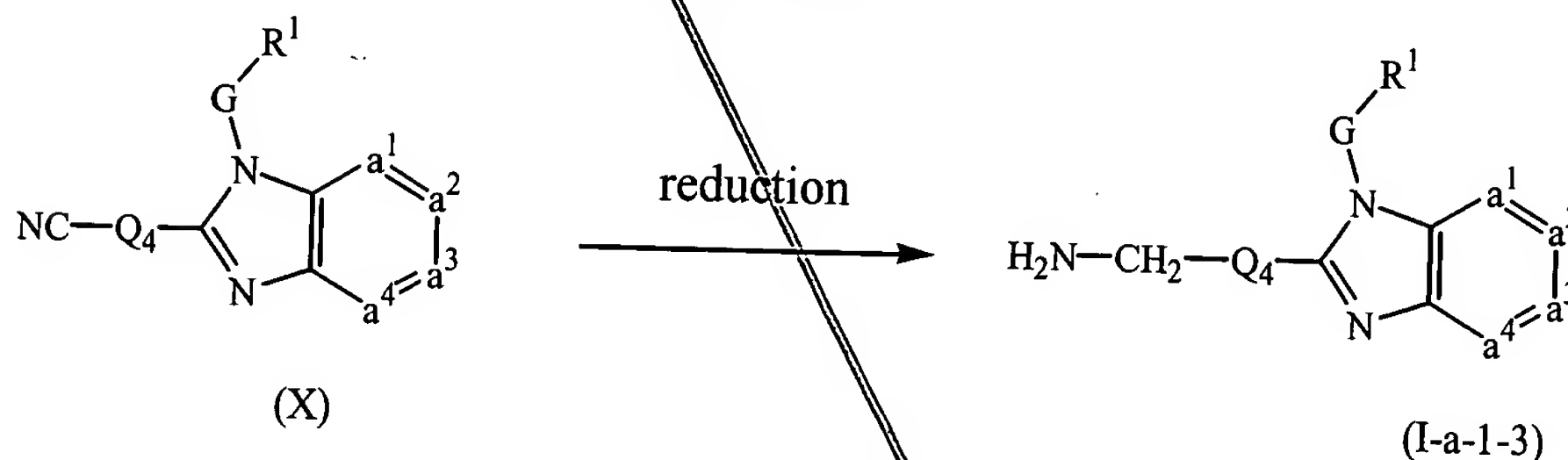
g) amination of an intermediate of formula (IX)

C1  
D1  
Cont



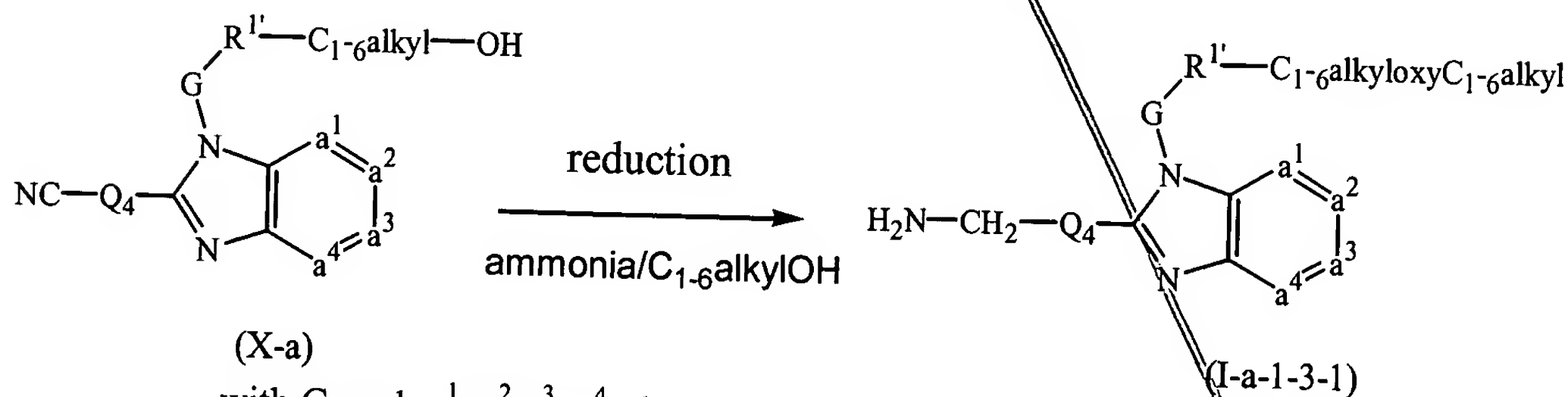
with  $R^1$ , G, and  $-a^1=a^2-a^3=a^4-$  defined as in claim 1, and  $H_2N-Q_3H$  being defined as Q according to claim 1 provided that both  $R^6$  substituents are hydrogen or  $R^2$  and  $R^4$  are both hydrogen, and the carbon adjacent to the nitrogen carrying the  $R^6$ , or  $R^2$  and  $R^4$  substituents contains at least one hydrogen, in the presence of a **suitable** an amination reagent;

h) reducing an intermediate of formula (X)



with  $R^1$ , G, and  $-a^1=a^2-a^3=a^4-$  defined as in claim 1, and  $H_2N-CH_2-Q_4$  being defined as Q according to claim 1 provided that Q comprises a  $-CH_2-NH_2$  moiety, in the presence of a **suitable** reducing agent;

i) reducing an intermediate of formula (X-a)

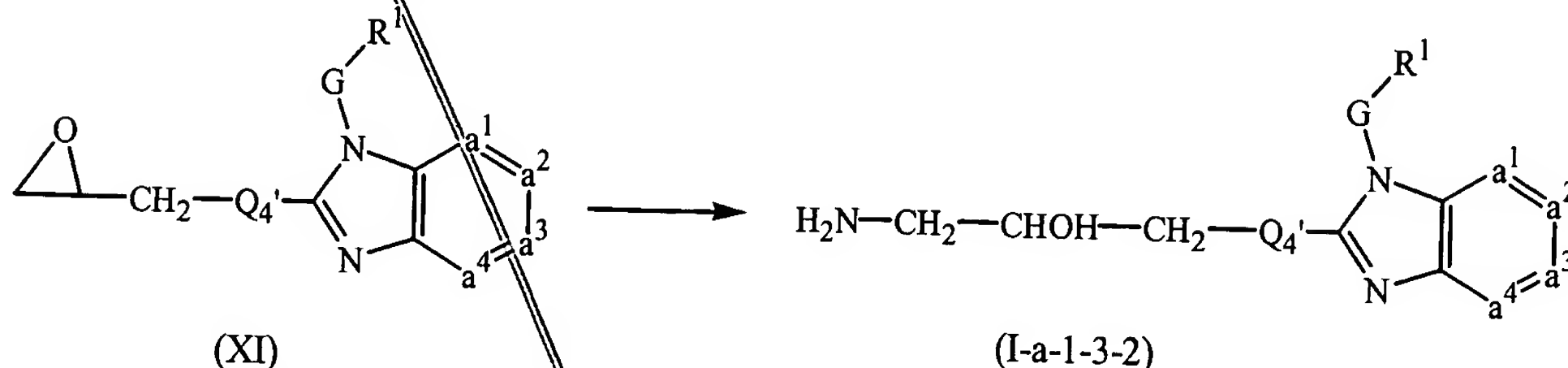


with G, and  $-a^1=a^2-a^3=a^4-$  defined as in claim 1,  $H_2N-CH_2-Q_4$  being defined as Q according to claim 1 provided that Q comprises a  $-CH_2-NH_2$  moiety, and  $R^{1'}$

C1  
D1  
Cont

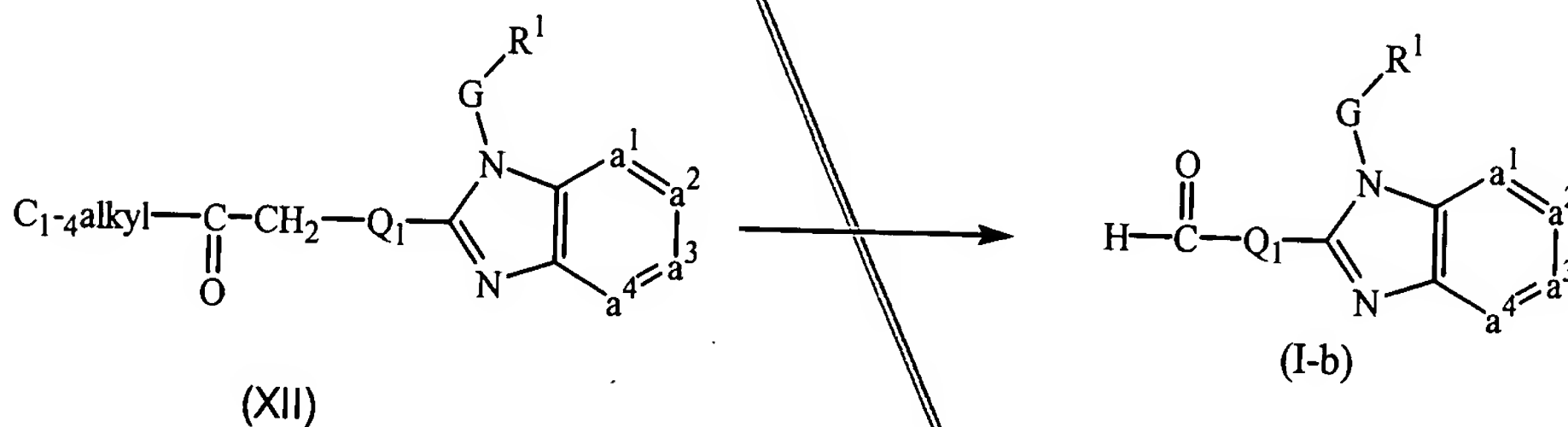
being defined as  $R^1$  according to claim 1 provided that it comprises at least one substituent, in the presence of a **suitable** reducing agent and **suitable** solvent;

j) amination of an intermediate of formula (XI)



with  $R^1$ , G, and  $-a^1=a^2-a^3=a^4-$  defined as in claim 1, and  $H_2N-CH_2-CHOH-CH_2-Q_4'$  being defined as Q according to claim 1 provided that Q comprises a  $CH_2-CHOH-CH_2-NH_2$  moiety, in the presence of **a-suitable** an amination reagent;

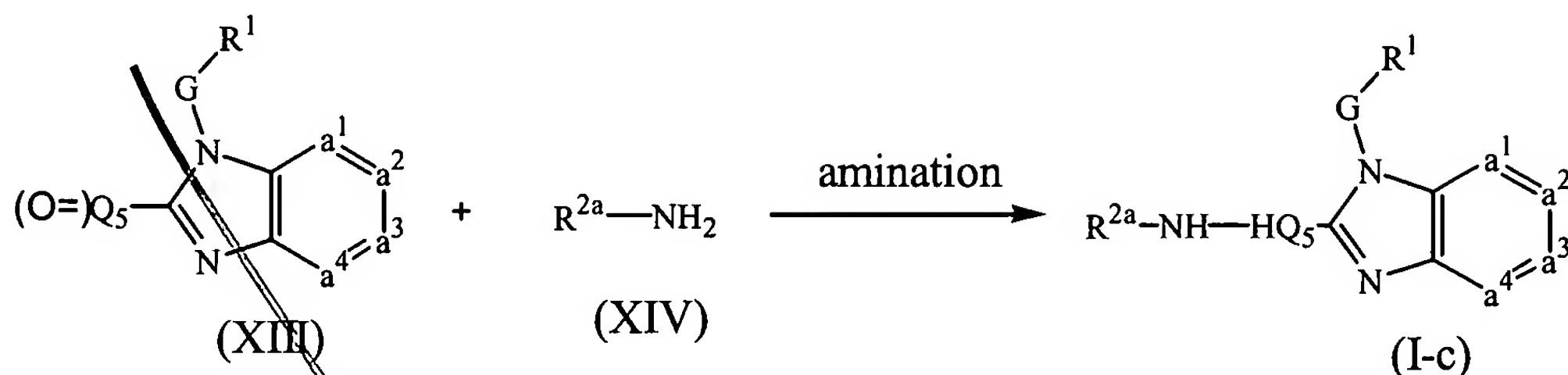
k) reacting an intermediate of formula (XII) with formic acid, formamide and ammonia



with  $R^1$ , G, and  $-a^1=a^2-a^3=a^4-$  defined as in claim 1, and  $H-C(=O)-Q_1$  being defined as Q according to claim 1 provided that  $R^2$  or at least one  $R^6$  substituent is formyl;

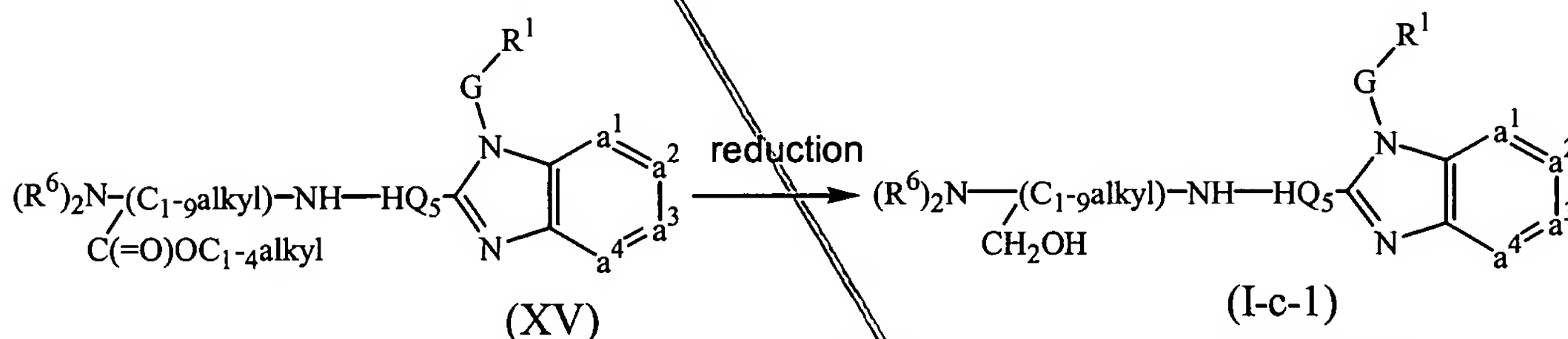
l) amination of an intermediate of formula (XIII) by reaction with an intermediate of formula (XIV)

C1  
 D1  
 Cont



with R<sup>1</sup>, G, and -a<sup>1</sup>=a<sup>2</sup>-a<sup>3</sup>=a<sup>4</sup>- defined as in claim 1, and R<sup>2a</sup>-NH-HQ<sub>5</sub> being defined as Q according to claim 1 provided that R<sup>2</sup> is other than hydrogen and is represented by R<sup>2a</sup>, R<sup>4</sup> is hydrogen, and the carbon atom adjacent to the nitrogen atom carrying the R<sup>2</sup> and R<sup>4</sup> substituents, carries also at least one hydrogen atom, in the presence of a **suitable** reducing agent;

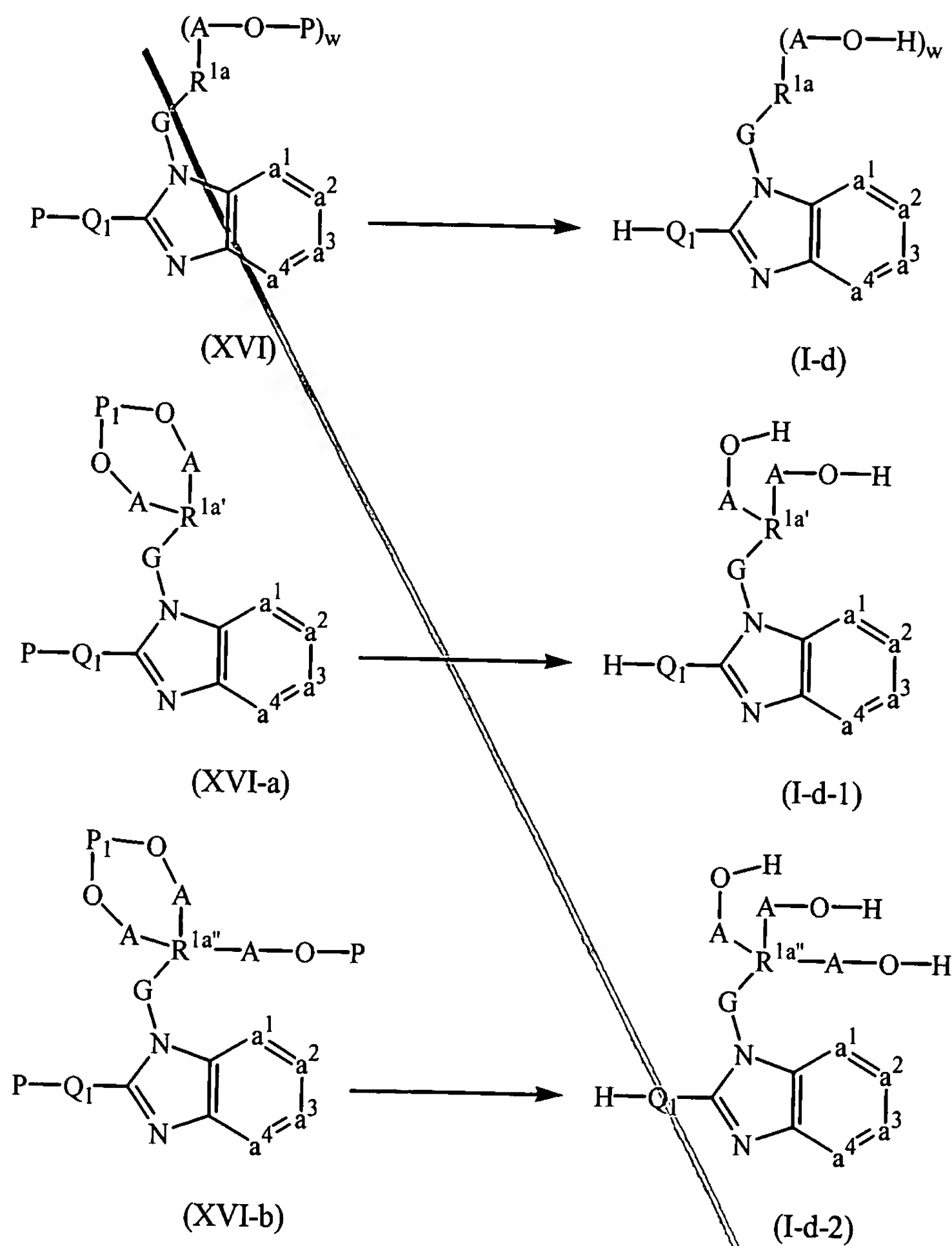
m) reducing an intermediate of formula (XV)



with R<sup>1</sup>, G, and -a<sup>1</sup>=a<sup>2</sup>-a<sup>3</sup>=a<sup>4</sup>- defined as in claim 1, and (R<sup>6</sup>)<sub>2</sub>N-[(C<sub>1-9</sub>alkyl)CH<sub>2</sub>OH]-NH-HQ<sub>5</sub> being defined as Q according to claim 1 provided that R<sup>2</sup> is other than hydrogen and is represented by C<sub>1-10</sub>alkyl substituted with N(R<sub>6</sub>)<sub>2</sub> and with hydroxy, and the carbon atom carrying the hydroxy, carries also two hydrogen atoms, and provided that R<sup>4</sup> is hydrogen, and the carbon atom adjacent to the nitrogen atom carrying the R<sup>2</sup> and R<sup>4</sup> substituents, carries also at least one hydrogen atom, with a **suitable** reducing agent;

n) deprotecting an intermediate of formula (XVI), (XVI-a) or (XVI-b)

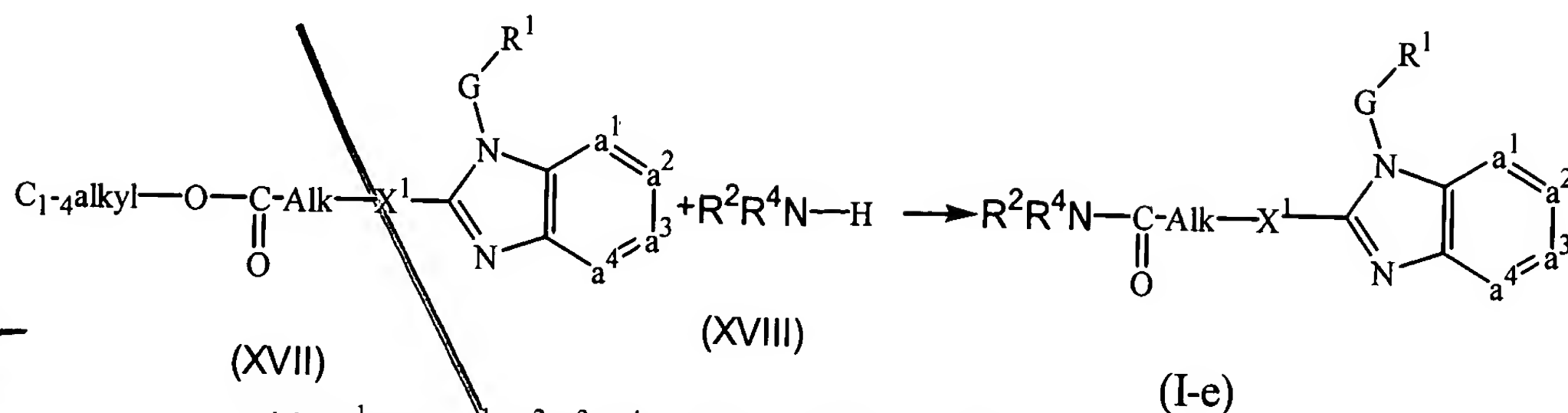
C1  
 Cont



with  $G$ , and  $-a^1=a^2-a^3=a^4-$  defined as in claim 1, and  $H-Q_1$  being defined as  $Q$  according to claim 1 provided that  $R^2$  or at least one  $R^6$  substituent is hydrogen, and  $R^{1a}-(A-O-H)_w$ ,  $R^{1a'}-(A-O-H)_2$  and  $R^{1a''}-(A-O-H)_3$  being defined as  $R^1$  according to claim 1 provided that  $R^1$  is substituted with hydroxy, hydroxy $C_{1-6}$ alkyl, or  $HO(-CH_2-CH_2-O)_n-$ , with  $w$  being an integer from 1 to 4 and  $P$  or  $P_1$  being a suitable protecting group, with a suitable acid;

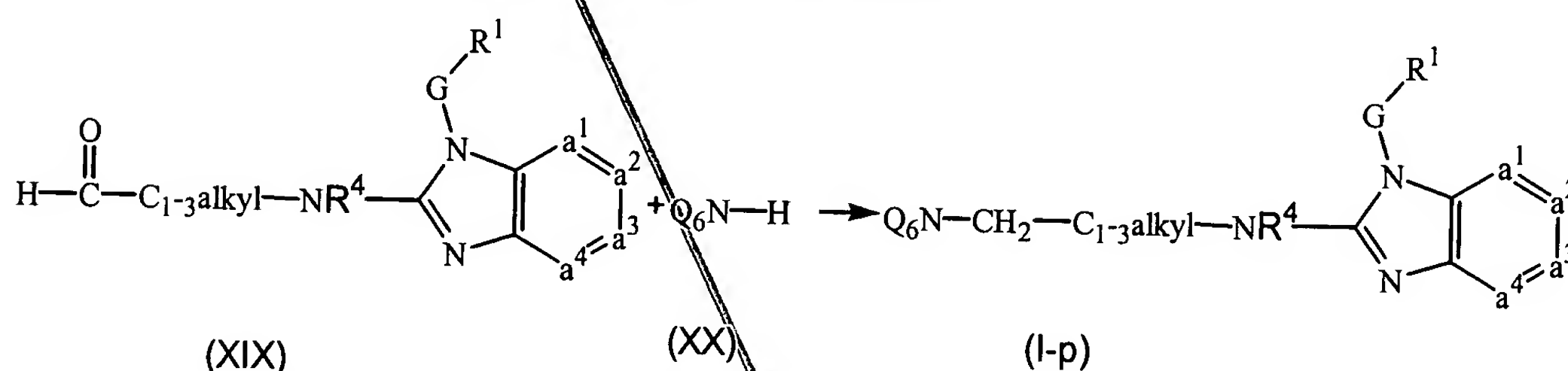
- o) amination of an intermediate of formula (XVII)

C1  
D1  
cont



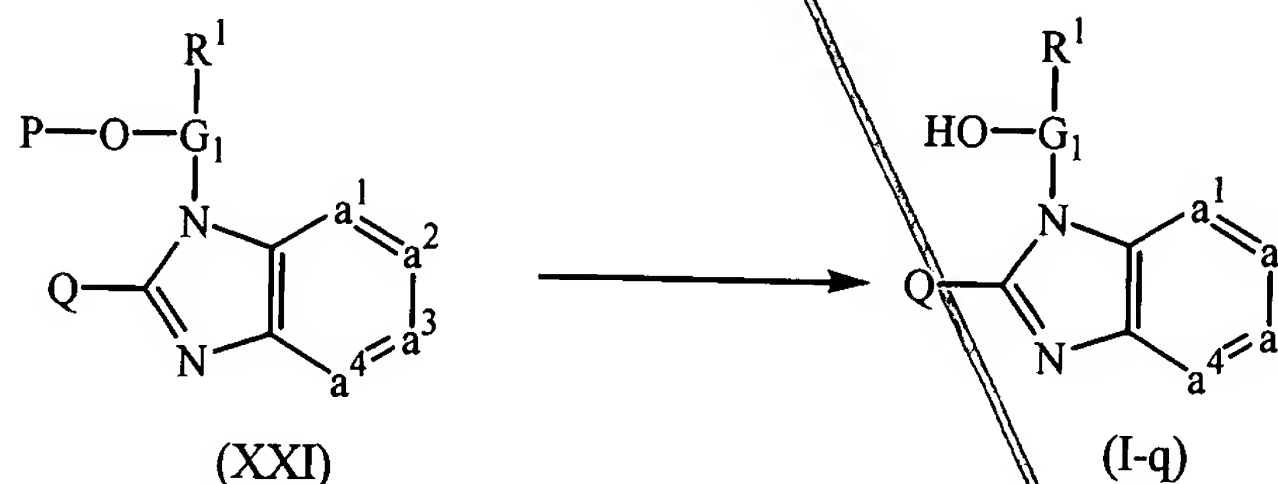
with  $\text{R}^1$ , G,  $-\text{a}^1=\text{a}^2-\text{a}^3=\text{a}^4-$ , Alk,  $\text{X}^1$ ,  $\text{R}^2$  and  $\text{R}^4$  defined as in claim 1, in the presence of a suitable amination agent;

p) amination of an intermediate of formula (XIX)



with  $\text{R}^1$ , G, and  $-\text{a}^1=\text{a}^2-\text{a}^3=\text{a}^4-$  defined as in claim 1, and  $\text{Q}_6\text{N}-\text{CH}_2-\text{C}_{1-3}\text{alkyl}-\text{NR}^4$  being defined as Q according to claim 1 provided that in the definition of Q,  $\text{X}^2$  is  $\text{C}_{2-4}\text{alkyl}-\text{NR}^4$ , in the presence of a suitable an amination agent;

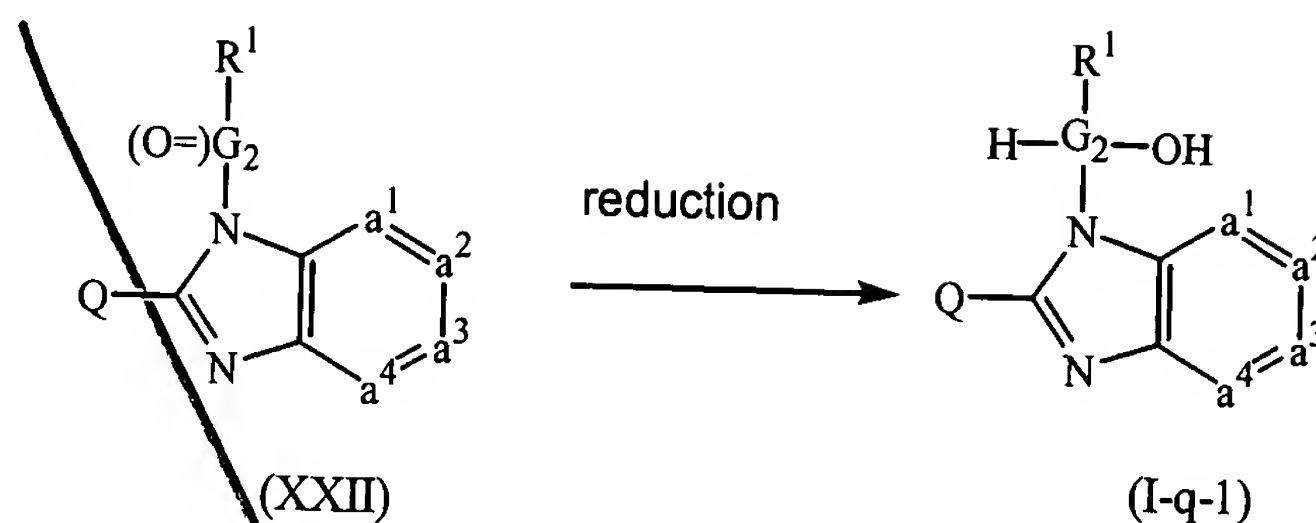
q) deprotecting an intermediate of formula (XXI)



with  $\text{R}^1$ , Q, and  $-\text{a}^1=\text{a}^2-\text{a}^3=\text{a}^4-$  defined as in claim 1, and  $\text{HO}-\text{G}_1$  being defined as G according to claim 1 provided that G is substituted with hydroxy or  $\text{HO}-(\text{CH}_2\text{CH}_2\text{O})_n$ ; and

r) reducing an intermediate of formula (XXII)

C1  
D1  
cont



with  $R^1$ , Q, and  $-a^1=a^2-a^3=a^4-$  defined as in claim 1, and H-G<sub>2</sub>-OH being defined as G according to claim 1 provided that G is substituted with hydroxy and the carbon atom carrying the hydroxy substituent carries also at least one hydrogen, in the presence of a **suitable** reducing agent.

16. (previously amended) A product, comprising:

- (a) a first compound as claimed in claim 1; and
- (b) a second antiviral compound,

wherein said first compound and said second compound are simultaneously, separately or sequentially used in the treatment or the prevention of viral infections.

17. (previously amended) A pharmaceutical composition, comprising:

- (a) a pharmaceutically acceptable carrier; and
- (b) as active ingredients:
  - i. a first compound as claimed in claim 1; and
  - ii. a second antiviral compound.

18. (previously added) The process of claim 15, further comprising the step of converting compound of formula (I'), stereochemically isomeric forms, metal complexes, quaternary amines or N-oxide forms thereof, into a therapeutically active non-toxic acid addition salt by treatment with an acid.

DOCKET NO.: JANS-0026 (JAB-1499 US)

Application No.: 10/019,380

Office Action Dated: April 18, 2003

PATENT

C1  
D1  
cont 19. (previously added) The process of claim 15, further comprising the step of converting compound of formula (I'), stereochemically isomeric forms, metal complexes, quaternary amines or *N*-oxide forms thereof, into a therapeutically active non-toxic base addition salt by treatment with alkali.

20. (previously added) The process of claim 15, further comprising the step of converting the acid addition salt form of compound of formula (I'), stereochemically isomeric forms, metal complexes, quaternary amines or *N*-oxide forms thereof, into the free base by treatment with alkali.

21. (previously added) The process of claim 15, further comprising the step of converting the base addition salt form of compound of formula (I'), stereochemically isomeric forms, metal complexes, quaternary amines or *N*-oxide forms thereof, into the free acid by treatment with acid.

22. (new) The process of claim 15, further comprising the step of converting said compound of formula (I'), stereochemically isomeric form, metal complex, quaternary amine or *N*-oxide form thereof, into a different form of compound of formula (I'), stereochemically isomeric form, metal complex, quaternary amine or *N*-oxide form thereof.